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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/497,943	02/04/2000	Mark Aaron Behlke		8098

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EXAMINER

SISSON, BRADLEY L

ART UNIT PAPER NUMBER

1634

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/497,943	Applicant(s) BEHLKE ET AL.	
	Examiner Bradley L. Sisson	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-33, 35, 37-41, 43-48, 55, 56 and 58-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Specification

1. The objection to the specification as it relates to the usage of trademarks has been withdrawn in view of the amendments to the specification.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 29-33, 35, 37-41, 43-48, 55, 56, and 58-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter

4. The instant application was filed on 04 February 2000 with claims 1-54 pending. A review of the original specification, including a review of original claims 1-54, fails to find the first instance of the transitional phrase "consisting essentially of" in the specification, much less use of said transitional phrase in the context of modifying one or more nucleic acids. A review of the amendments finds the first use of said phrase in the amendment received 14 January 2005. Page 8 of the response received 14 January 2005 identifies which claims this amendment was to,

Art Unit: 1634

and asserts at page 9 “The amendments are fully supported by the application as filed and introduces no new matter.” The amendment of 22 July 2005 introduces said phrase at additional instances, and again, the accompanying remarks of applicant’s representative fails to identify just where in the original disclosure support for this amendment is to be found. As set forth in MPEP 714.02 [R-2]:

The prompt development of a clear issue requires that the replies of the applicant meet the objections to and rejections of the claims. Applicant should also specifically point out the support for any amendments made to the disclosure. See MPEP § 2163.06.”(Emphasis added.)

5. In the instant application applicant’s representative has made repeated amendments to claims and has not provided an indication where support for the newly added limitation is to be found. In the absence of convincing evidence to the contrary, the insertion of the phrase “consisting essentially of” is deemed new matter and as such, claims 29-33, 35, 37-41, 43-48, 55, 56, and 58-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Written Description

6. The claims are drawn to a method whereby any of a large population of partially complementary sequences can be labeled and ultimately be rendered detectable. While the claims and indeed the original specification teach various ranges of lengths of components of the first and second oligonucleotides and statements have been made as to the type and form of modified nucleotide contained therein, the specification has not provided such full, clear, and concise description of those first and second polynucleotides such that one skilled in the art

Art Unit: 1634

would be able to recognize those that have utility from those that do not. It is not enough that one be able to detect a nucleic acid for the nucleic acid detected must have utility. While some nucleic acids meet this utility requirement, the specification does not contain an adequate written description of just which first and second oligonucleotides meet this requirement. Accordingly, and in the absence of convincing evidence to the contrary, claims 29-33, 35, 37-41, 43-48, 55, 56, and 58-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Utility

7. Claims 29-33, 35, 37-41, 43-48, 55, 56, and 58-64 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

8. Satisfaction of the utility requirement can be achieved either directly from the method of downstream therefrom. In the instant case the claims are drawn to a method whereby any of a large population of partially complementary sequences can be labeled and ultimately be rendered detectable. Satisfaction of the utility requirement is not achieved by simply labeling and/or detecting any nucleic acid as not all nucleic acids have utility. Consequently, the labeling and detection must be linked to a nucleic acid that does satisfy the utility requirement.

9. As presently worded, the claimed method fairly encompasses the labeling (and detection) of nucleic acids for which no known function has been identified, e.g., expressed sequence tags, or ESTs.

Art Unit: 1634

10. To the degree that the instant disclosure provides adequate written support, applicant is urged to consider narrowing the claims to where the method results in the labeling of useful oligonucleotides.

11. Claims 29-33, 35, 37-41, 43-48, 55, 56, and 58-64 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 30 is indefinite as to how a nucleotide can comprise the first or second oligonucleotides. Applicant is urged to consider wording more along the lines of that found in claim 31.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1634

16. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 29-33, 35, 37, 38, 40-41, 43-46, 55, 56, and 58-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,882,856 (Shuber) in view of US Patent 6,248,568 B1 (Khan et al.), US Patent 5,989,871 (Grossman et al.), and WO 93/05175 (Brown).

19. Shuber, column 2, third paragraph, and column 4, third paragraph, disclose the use of a chimeric primer that is described as being configured 5'-XY-3'. The "X" domain "comprises a sequence within or flanking the target sequence or its complement." The "Y" domain "comprises a sequence contained within or flanking the target sequence or its complement." Accordingly, the "X" domain meets the limitations of applicant's "Signal Template Domain" and the "Y" domain meets a limitation of the "Substrate Hybridization Domain" of the "first

Art Unit: 1634

oligonucleotide.” The target sequence meets a limitation of applicant’s second sequence wherein that portion of the target sequence that hybridizes to the Template Hybridization Domain meets a limitation of applicant’s Substrate Hybridization Domain, and that portion of the target sequence located in the 5’ direction of the Substrate Hybridization Domain meets a limitation of applicant’s Substrate Template Domain. As seen in column 4, the respective domains may be comprised of nearly any nucleotide sequence and that it can range in length from about 17 to about 25 bases.

20. Shuber does not teach adding a labeled nucleotide to the end of the Template Hybridization Domain, thereby forming a Signal Domain.

21. Khan et al., column 5, disclose the incorporation of labeled (modified) nucleotides into primer extension products, and that said modified nucleotides could be chain terminating. Also disclosed are a plethora of various labels that can be incorporated. Such labels include, but are not limited to radioactive, fluorescent, biotin, modified ribose or phosphate groups, esters, and the like.

22. While Khan has not been found to recite the specific activity limitation of claims 55 and 56, such activity is considered to be the result of routine optimization and does not rise to the level of a patentable distinction.

23. Neither Shuber nor Khan et al., have been found to teach of generating homopolymeric tails.

24. Grossman et al., column 19, discloses the generation of homopolymeric tails. Also disclosed is the use of a detectable nucleotide, e.g., fluorophore (applicant’s fluorescein).

Art Unit: 1634

25. Brown et al., disclose the use of 2,6-diaminopurine in oligonucleotides and their use in primer extension reactions.

26. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the procedure of Shuber whereby the chimeric primer was used in a primer-extension method whereby the extension of said primer resulted in a labeled nucleotide being incorporated at the 3' terminus, thereby forming a Signal Domain. In view of the detailed teaching of suitable labels and alternative nucleotides that the primer could comprise, the skilled artisan would have been amply motivated to have selected any one or combination of labels disclosed in the art of record (Khan et al., and Grossman et al.) as such would have allowed the ordinary artisan the ability to directly and more readily detect the presence of a Signal Domain.

27. Attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. *In re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; *In re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. *In re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; *In re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. *In re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; *In re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; *In re Irmischer*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

Art Unit: 1634

28. For the above reasons, and in the absence of convincing evidence to the contrary, claims 29-33, 35, 37, 38, 40-41, 43-46, 55, 56, and 58-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,882,856 (Shuber) in view of US Patent 6,248,568 B1 (Khan et al.), US Patent 5,989,871 (Grossman et al.), and WO 93/05175 (Brown).

Conclusion

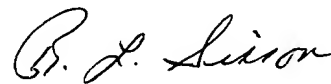
29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

31. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

Art Unit: 1634

system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
14 October 2005